

REMARKS

In this paper, claims 4 and 5 are amended to correct minor informalities. No new matter has been introduced.

Upon entry of this paper, claims 7 and 8 are pending in this application, whereas claims 1 – 6, and 11 – 14 have been withdrawn, and claims 9 – 10 have been canceled.

Amendment to or cancellation of any claim herein is not to be construed as acquiescence to any of the rejections/objections set forth in the Office Action, and was done solely to expedite prosecution of the application.

Applicant respectfully reserves the right to pursue any non-elected, withdrawn, canceled or otherwise unclaimed subject matter in one or more continuation, continuation-in-part, or divisional applications.

Reconsideration and withdrawal of the rejections of this application in view of the amendments and remarks herewith, is respectfully requested, as the application is in condition for allowance.

Finality Of the Action

Applicant notes with appreciation that the Examiner acknowledged Applicant's filing of a Request for Continued Examination (RCE) and also commented that this application was eligible for continued examination under 37 CFR 1.114 (page 2 of the Action). Applicant hereby thanks the Examiner for her decision to withdraw the finality of the previous Office action.

Nevertheless, it is noted that the Office has now made final of the present Action. It is contended that the finality of the Action is improper and premature pursuant to MPEP 706.07(b). Contrary to the Office's assertion at page 5 of Action that "the same references as used in the previous Office Action have been cited for the new rejections," Applicant submits that the Tropepe reference (Sc. 287: 2032-2036, 2000; hereinafter "Tropepe") cited in the present Action had not been cited in the previous Office Action. As such, Applicant submits that it is improper for the Office to make final of this Action.

Therefore, reconsideration then withdrawal of the finality of the present Action is proper and the same is requested.

Claim Rejection under 35 U.S.C. §103(a)

Claims 7 and 8 are rejected under 35 U.S.C. 103(a) as allegedly unpatentable over Haruta *et al.* (Nat Neurosc 4: 1163-1164, 2001; hereinafter “Haruta”) in view of Tropepe and in further view of Kosaka *et al.* (Exp Cell Res 245: 245-251, 1998; hereinafter “Kosaka”). In particular, the Office asserts that Haruta teaches proliferation of iris-derived cells (from iris tissue of adult rats) in serum free medium into cells that are positive for neurofilament 200, and that ciliary margin cells can differentiate to rod photoreceptors subsequent to spherical colony formation (page 4 of the Action). The Office then asserts that Haruta suggests differentiation to rod photoreceptors that are rhodopsin positive without a gene transfer. The Office also asserts that Tropepe teaches formation of spherical colonies as a result of culture of the ciliary derived cells. Although the Office concedes that the combination of Haruta and Tropepe fails in teaching specifics of the culture medium as recited in the present claims, the Office nevertheless asserts that Kosaka makes up for such deficiencies (see pages 4 & 5 of the Action). The rejection is hereby traversed.

To properly determine a *prima facie* case of obviousness, the Examiner “must step backward in time and into the shoes worn by the hypothetical ‘person of ordinary skill in the art’ when the invention was unknown and just before it was made.” M.P.E.P. § 2142. This is important as “impermissible hindsight must be avoided and the legal conclusion must be gleaned from the prior art.” *Id.* Three criteria may be helpful in determining whether claimed subject matter is obvious under 103(a): first, if there is some suggestion or motivation to modify or combine the cited references; second, if there is a reasonable expectation of success; and third, if the prior art references teach or suggest all the claim limitations. *KSR Int'l Co. v. Teleflex, Inc.* No 04-1350 (U.S. Apr. 30, 2007). With regard to the first criterion, the mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination. *In re Mills*, 916 F.3d 690 (Fed. Cir. 1990). “Knowledge in the prior art of every element of a patent claim ... is not of itself sufficient to render claim obvious.” *Graham v. John Deere Co.*, 383 U.S. 1, 17-18 (1966); *Teleflex, Inc. v. Ficosa N. Am. Corp.*, 299 F.3d 1313, 1333-34 (Fed. Cir.

2002)]. The issue is whether there is an apparent reason to combine the known elements in the fashion claimed by the patent at issue. *KSR Int'l Co. v. Teleflex, Inc.*

The present invention is directed to a method for producing rhodopsin-positive retinal nerve cells comprising: isolating iris pigmented epithelial cells from an eyeball; and performing adherent culturing of the iris pigmented epithelial cells with a serum-free culture medium so as to induce differentiation of the iris pigmented epithelial cells into the rhodopsin-positive retinal nerve cells, wherein the iris pigmented epithelial cells have not been subjected to a gene transfer, the serum-free culture medium when the adherent culturing starts contains at least one of a fibroblast growth factor 2, a fibroblast growth factor 9, and a ciliary neurotrophic factor with a concentration in a range of 1 to 100 ng/mL, the iris pigmented epithelial cells in the serum-free culture medium when the adherent culturing starts have a cell density of 1×10^5 cells/cm² or less, and the serum-free culture medium is a DMEM/F12 culture medium, a DMEM culture medium, or an EMEM culture medium (see claim 7).

Applicant argues that the combination of Haruta, Tropepe, and Kosaka does not teach the presently claimed subject matter. For example, none of the cited references teaches inducing differentiation of *iris pigmented epithelial cells* into the *rhodopsin-positive* retinal nerve cells *without a gene transfer*. In contrary to the Office's assertion, Applicant submits that the method disclosed in Haruta for differentiating iris-derived cells into photoreceptors expressly requires a transfer of Crx genes, evidenced by all the studies in Haruta demonstrating that the inductive effects of Crx are essential for the iris-derived cells to become rhodopsin-positive. Although Haruta considers briefly the possibility of development of the iris-derived cells into photoreceptors without a gene transfer, a skilled artisan would appreciate that the iris derived cells cannot be differentiated into rhodopsin positive cells such as photoreceptors without a gene transfer based on Haruta's express teaching. Applicant contends that Haruta provides at most an unfounded guess on the possibility of gene transfer (or without), for which it does not present any method or test results. Indeed, one skilled in the art could properly consider that Haruta fails in teaching or suggesting differentiation of iris derived cells into rhodopsin-positive retinal nerve cells without a gene transfer.

Applicant further submits that the addition of Tropepe also fails in teaching or suggesting the features of the present invention. Specifically, Tropepe does not teach or suggest differentiation of the iris pigmented epithelial cells into the rhodopsin-positive retinal nerve cells. Furthermore, in contrast to the Office's assertion, Tropepe does not teach or suggest that its spherical colonies can be obtained as a result of culturing the ciliary derived cells (of the adult mice). Tropepe states expressly that "[i]n addition, colonies **did not** arise from cells of the adult iris, ciliary muscle, or NR or from nonpigmented ciliary process cells in any of the species tested." (see para. 2, col. 1, p. 2033 of Tropepe). Indeed, one skilled in the art would agree that Tropepe does not teach or suggest that its spherical colonies can be obtained through culturing the ciliary derived cells, let alone differentiation of *iris pigmented epithelial cells* to *rhodopsin-positive cells* without a gene transfer.

Moreover, Applicant submits that the addition of Kosaka does not cure the deficiencies of Haruta and/or Tropepe. Kosaka only teaches additionally medium and culture conditions. Kosaka does not teach or suggest that any method of forming spherical colonies without a gene transfer, let alone a method of inducing differentiation of specific cells (i.e., the iris pigmented epithelial cells) into the rhodopsin-positive retinal nerve cells without a gene transfer. Applicant thus contends the combination of Haruta, Tropepe and Kosaka still fails in teaching or suggesting each and every element of the presently claimed subject matter.

Applicant further contends that one skilled in the art would not be motivated to modify the methods disclosed in the art for the purpose to differentiate the iris pigmented epithelial cells (IPE cells) into the *rhodopsin-positive* retinal nerve cells without a gene transfer (as the presently claimed method does). None of the cited references teaches differentiation of iris derived cells into rhodopsin positive cells without a gene transfer. Instead, a skilled artisan would consider that the disclosure of Tropepe indeed teaches away from such a possibility (as above discussed). Based on the disclosure of the cited art, Applicant contends that a skilled artisan could not possibly **predict** that IPE cells can be differentiated into rhodopsin-positive retinal nerve cells at the time of the invention. Even *assuming* that one chooses to make a guess in this regard, there is no reasonable expectation of success to arrive at the present

invention based on the existing information and knowledge in the art (such as, the test results in Haruta, and source information on the spherical colonies in Tropepe).

As such, Applicant submits that the presently claimed subject matter is clearly patentable over Haruta and Tropepe in view of Kosaka, at least due to the reasons as follows: first of all, the combination of the cited references still fails in teaching or disclosing each and every element of the presently claimed subject matter; second, none of the cited references provides any specific suggestion or motivation to a skilled artisan to make a modification in order to arrive at the present invention; and finally, there is no reasonable expectation of success in the field to arrive at the present invention.

Therefore, reconsideration then withdrawal of the rejection under 35 U.S.C. § 103(a) over Haruta and Tropepe in view of Kosaka is proper and the same is requested.

CONCLUSION

In view of the remarks made herein, the present application is believed to be in condition for allowance. Favorable reconsideration of the application and prompt issuance of a Notice of Allowance are respectfully requested. If the Examiner believes that a telephone conversation with Applicant's attorney/agent would expedite prosecution of this application, the Examiner is cordially invited to call the undersigned attorney.

Although it is not believed that any further fee is needed to consider this submission, the Office is hereby authorized to charge our deposit account **04-1105** under Order No. 64603 (70904), should such fee be deemed necessary.

Dated: May 3, 2010

Respectfully submitted,

Customer No. 21874

By Weiying Yang/
Weiying Yang, Esq.
Registration No.: 61,637
EDWARDS ANGELL PALMER & DODGE
LLP
P.O. Box 55874
Boston, Massachusetts 02205
(617) 239-0416
Attorneys/Agents For Applicant